

REMARKS

Reconsideration and withdrawal of the rejections of the claimed invention is respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 13-15, 21-23, 27, 28, 47-52, 57, 58 and 74 are pending in this application. No new matter has been added by this amendment.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. THE 35 U.S.C. 103(a) REJECTION HAS BEEN OVERCOME

Claims 13-15, 21-23, 27, 28, 47-52, 57, 58 and 74 were rejected as allegedly being obvious by Ruegg et al. (US 6,180,563). The applicants request reconsideration of this rejection for the following reasons.

The applicants respond to the "Response to Applicants' Arguments" section of the Office Action as it shows a clear error in the application of the standards for determining *prima facie* obviousness and for re-establishing a case for obviousness in light of the applicants' previous arguments (for convenience sake, the previous response is repeated at the end of the current response). The reasons for asserting clear error is as follows:

1. Determinations of *prima facie* obviousness require consideration of both the applicants' invention as a whole and the prior art reference as a whole. While the applicants' invention contemplates that the combination of a glufosinate-type herbicide (herbicide (A1)) with and herbicide of (B1) such as metolachlor; (B2) such as bispyribac or its salts, and pyriothobac or its salts; or (B4) sethoxydim and clethodim would result in unexpectedly superior activity against harmful plants in cotton crops, there is nothing within Ruegg which makes a similar suggestion.

Even the reasoning for a routine combination of herbicides without consideration of unexpected results is in error as it is clear that an as a whole reading of Ruegg would focus on

trifloxysulfuron as the active ingredient to which additional herbicides may be combined, i.e. a completely different combination than the applicants' claimed invention.

The applicants' use of the transitional term "comprising" does not excuse the Examiner from making the as a whole consideration of the Ruegg reference.

2. Ruegg specifically names glufosinate, metolachlor, pyriithobac, sethoxydim and clethodim, but only in the context of combination with a trifloxysulfuron. There is no indication that combination of these specifically named herbicides (and more specifically, a glufosinate-type herbicide with metolachlor, bispyribac, pyriithobac, sethoxydim or clethodim) with each other in the absence of trifluoxysulfuron would provide unexpected results against harmful plants.

3. During the discussion of the applicants' unexpected results, three clear errors were made in the response. First, the data with respect to the combination of glufosinate-ammonium (A1.2) with metolachlor (B1.9) was stated to be unexpected because the experimental result against *Datura Stramonium* was 97% instead of the expected 75% whereas the same combination against *Echinocloa* was "only" 94% instead of the expected 88%. However, there is no minimum increase for what would be considered to be "unexpected" by one of ordinary skill in the art.

Second, the expected activities in the examples are theoretical maximums established by well-known methods in the art, i.e. application of the Colby equation. One of ordinary skill in the art would not have expected ANY increase beyond these theoretical maximums and therefore the 6% increase for *Echinocloa* would have been unexpected to one of ordinary skill in the art.

Third, while the applicants have provided test data and described the methodology for establishing synergism (see page 28, lines 7-22 of the specification), the Examiner provides no evidence which supports his statement that "small increases over unexpected results are questionable and are not totally convincing." or contradicts the positions which the applicants have presented. Moreover, "totally convincing" is not the standard in order to overcome a preliminary holding of *prima facie* obviousness. All that is required is that a preponderance of the evidence favors non-obviousness (e.g. if the evidence was 51% in favor of non-obviousness and 49% in favor of obviousness, then the rejection cannot be allowed to stand).

4. Applicants note that claims 14, 15, 22 and 23 (method claims) and claims 28, 29, 51 and 52 (composition claims) are specifically directed toward metolachlor or pyriithobac as herbicide (B).

For any of the above reasons, the obviousness rejection is in clear error and should be withdrawn.

(Copy of response from 7 December 2007)

Background

The applicants maintain their position from the previous office action, but since this was unpersuasive, the applicants will try to present the argument in a different manner to hopefully better explain why the applicants believe the obviousness rejection to be in error.

By apparently fixating on finding the specific compounds of (A) and (B) within Ruegg, the rejection has lost sight of what is the applicants' invention when considering the applicants' invention and Ruegg as a whole.

While it is true that the use of the term "comprising" could conceivably encompass trifloxysulfuron, this is not the inventive step of the applicants' claimed invention, i.e., it is irrelevant what other compounds are encompassed by the term "comprising" so long as the combination of compounds of formula (A) with herbicides (B1) metolachlor, (B2) bispyribac or its salts, and pyriithiobac or its salts; or (B3) sethoxydim and clethodim produce synergistic effects in combatting harmful plants in cotton crops.

As stated in MPEP 2142 (Legal Concept of *Prima Facie* Obviousness) - "To reach a proper determination under 35 U.S.C. 103, the examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences," conduct the search and evaluate the "subject matter as a whole" of the invention."

Applying this concept to the facts of this case, the Examiner is stepping into the shoes of the person of ordinary skill in the art ***just before the applicants' invention was made***. When presented with the Ruegg reference, there would be a determination of what would be obvious variations of this invention and what does this reference teach as a whole.

Discussion regarding synergistic effects

When reading this reference without the benefit of the applicants' claims, it is clear that Ruegg is directed toward the use of glyphosate/glufosinate in combination with sulfonylureas (compound (I)) to produce synergistic effects. Other herbicides may be added to the combination, *so long as the combination of glyphosate/glufosinate in combination with sulfonylurea produce synergistic effects*. Nowhere in the disclosure of Ruegg is it suggested that combining glyphosate/glufosinate with other herbicides such as (B1) metolachlor, (B2) bispyribac or its salts, and pyriothiac or its salts; or (B3) sethoxydim and clethodim would produce synergistic effects in combatting harmful plants in cotton crops.¹

The Office Action appears to acknowledge that Ruegg does not teach synergistic effects for the combinations claimed by the applicants by acknowledging that the applicants' did provide "...unexpected results for the above combination of ingredients as shown on pages 31-35 of the specification." (page 3, 3rd and 4th line from bottom of page). However, the unexpected results were not given their proper weight as it was alleged that the unexpected results are for specific application rates of each herbicide, i.e. there is no basis or evidence provided which supports the position that specific application rates are a necessary element of the claim or is not within the practicable skill of those in the art. As noted by in the Office Action, Ruegg recited broad application rates in their specification (which was not necessary to be included in their claims) for their own combination of herbicides and it is clear that some amount of experimentation with application rate parameters is permitted within the art once it is known which herbicides to select.

The key to the invention which Ruegg does not teach is the combination of glyphosate/glufosinate in combination with sulfonylurea produce synergistic effects; only the applicants provide this teaching. However, once provided with this teaching, the skilled artisan is more than capable of determining the appropriate application rate absence evidence to the contrary.

¹ As a test of the Examiner's assertion of obviousness, the applicants suggest showing the Ruegg reference to a colleague who has never seen the applicants' claims before and ask them what they would consider to be obvious variants of the Ruegg reference after reading it without benefit of the applicants' claims. While they may suggest that additional herbicides could be added to the glyphosate/glufosinate with sulfonylurea combination, it is highly unlikely that they would glean that glyphosate/glufosinate + (B1) metolachlor, (B2) bispyribac or its salts, and pyriothiac or its salts; or (B3) sethoxydim and clethodim would produce synergistic effects especially in the absence of any evidence supporting synergy based on this combination.

Interpretation of Data is Incorrect

With regard to the conclusion that combining substances of the same utility with the expectation of at least an additive effect is incorrect. The additive effect is only a theoretical maximum which presumes that there is no competition between the substances to produce the effect or that no detrimental changes occur which might decrease the additive effect.²

Contrary to the assertion in the Office Action, an improvement according to the "additive method" is indicative of a clear synergism, even if the effect is only slightly above the level of the formal addition of the effects of the single active ingredients.

The latter conclusion is reliable because the herbicidal effect of a combination of two herbicides up to formal addition of the effects obtained by the single application of each active ingredient only is not what is expected by the person skilled in art.

Synergism requires a showing of more than an additive effect. Not only have the applicants shown this, the applicants have shown synergism even when assuming a perfect additive effect. Moreover, the Examiner is mistaken in asserting that small differences between theoretical maximum additive effects and the effects actually shown are not evidence of synergism. This is synergism on its face. In addition, at high levels of activity, even small increases beyond the theoretical maximum are surprising evidence of synergism.

For example, the effect of 450 g/ha glufosinate-ammonium (A1.2) and 930 g/ha metolachlor (B1.9) as shown in Table 2 (see page 32 of the specification) produced an effect which was 6% greater than the theoretical maximum additive effect (i.e. 94% vs. 88%). This effect is surprising because the effect of glufosinate-ammonium alone at 450 g/ha produces 0% effect.

Other measures of synergism such as the Colby equation (see page 28 of the specification)³ show lesser expectations of additive effects. For example, when assuming that

² As an illustration of this concept, think of an enzymatic reaction where Enzyme A and Enzyme B, which recognize the same active site, both have an activity of 50% on a substrate when used alone. Adding Enzyme A and Enzyme B to the substrate would still result in 50% activity (not 100%) because they would be competing for the same active site. Likewise, according to the logic of the Office Action, adding two herbicides which each have 100% activity, would result in the non-sensical conclusion that the resulting composition would have 200% activity.

³ $E = A+B-(A \cdot B/100)$

A, B = effect of a. i. A or B in % at a or b g a.i./ha, respectively;
E = expected effect of the combination in % at a+b g a.i./ha.

glufosinate-ammonium (A1.2) had some herbicidal effect (e.g. 5%), this and 930 g/ha metolachlor (B1.9) still had 88% activity, the additive effect is not 93% (5% + 88%) but only 88.6%. ($E = 5\% + 88\% - (5 \times 88/100)\% = 88.6\%$)

Likewise, in Table 5, the example with testing the combination of 400 g/ha glufosinate-ammonium (A1.2) + 105 g/ha pyriithiobac (B2.4) produces a herbicidal effect of 95% on Ipomoea, i.e. 10% above the effect obtained by calculation of the formal addition of the effects $43\% + 42\% = 85\%$. This increase of 10% action is a remarkable increase especially if compared with the expected effect of Colby which is calculated as follows:

$$E = 43\% + 42\% - (43 \cdot 42/100)\% = 85\% - 18,2\% = 66.8\%$$

Compared to expected effect calculated according to the Colby equation the increase up to 85% is thus an increase of more than 18 points, i.e. 27% more based on the expected effect of 66,8% ($18.2:66.8 \times 100\% = 27.2\%$).

The combination effect is thus clearly synergistic.

The Office Action appears to discount the evaluation method of Colby (see *Weeds* 15 (1967) S. 20 to 22 - copy provided with this office action and which was mentioned in the "Biological Examples" section of the specification), but offers no evidence which contradicts the finds from this peer-reviewed journal. The treatise of Colby and detailed findings therein makes it clear that the formal addition of herbicidal effects of the herbicidal components of a mixture cannot be expected for scientific reasons absent evidence to the contrary. The expected effect will always be below the formal addition of the herbicidal effects.

Lastly, while the applicants have provided evidence in support of synergism, there has been no countervailing evidence presented in any office action; only an unsupported opinion with regard to the applicants' evidence.

Therefore, Ruegg does not teach the inventive concept of the applicants claimed invention and the applicants have shown evidence of synergy and as such the applicants' claims are unobvious over Ruegg.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,
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